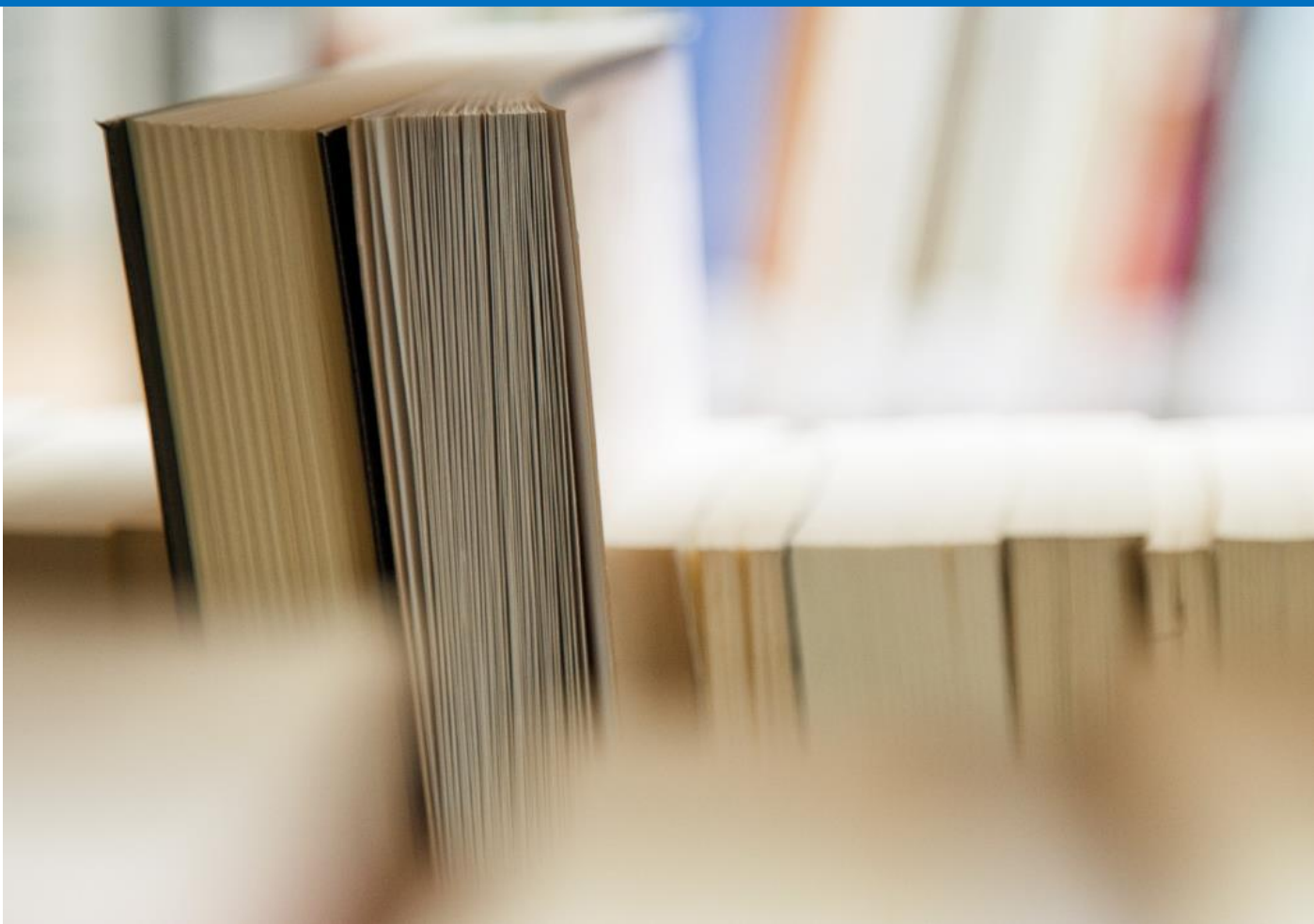




Pharmacology collections

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A- Drugs acting by enzyme inhibition

1- α -methyldopa : inhibits dopa-decarboxylase enzyme (Used in treatment of hypertension, it is the drug of choice in hypertension during pregnancy).

2-Anti-cholinesterase: either reversible as physostigmine and neostigmine, or irreversible as organophosphorous compounds.

3-Glucocorticoids (cortisone): inhibits phospholipase A2.

4-NSAIDS e.g. Aspirin, phenylbutazone, Diclofenac....., inhibit cyclooxygenase enzymes (COX).

5-Zileuton: inhibits 5-lipoxygenase enzyme $\rightarrow$ $\downarrow$ leukotriene synthesis, used in prophylaxis of bronchial asthma.

6-Dazoxiben: Antiplatelet by inhibition of thromboxane **A2** synthase (same mechanism as aspirin as antiplatelet).

7-Methylxanthines e.g. theophylline and aminophylline, inhibit P.D.E (phosphodiesterase) type IV (4) $\rightarrow$ $\uparrow$ c-AMP $\rightarrow$ CNS stimulation, cardiac stimulation, V.D. and bronchodilation.

8-Disodium cromoglycate and Nedocromil sodium: (mast cell stabilizers)

Used in prophylaxis of bronchial asthma, given by inhalation, inhibit P.D.E in mast cell.

9-Warfarin:

"oral anticoagulant", inhibits vitamin K reductase →

↓ Synthesis of prothrombin II (2) and other coagulation factors (VII, IX, X).

10-Dipyridamole: Antiplatelet, ↓ PDE → ↑ c-AMP.

11-pentoxifylline: methylxanthine, antiplatelet, as dipyridamole.

12-Statins: antihyperlipidaemics, ↓ HMG.CO.A reductase enzyme.

13-Carbonic anhydrase inhibitors: e.g. acetazolamide (diamox) used as diuretic (self-limiting), ↓ IOP in glaucoma, treatment of petit-mal epilepsy, as alkalinizer of urine.

14-Angiotensin converting enzyme (ACE) inhibitors:

e.g. captopril, lisinopril, enalapril, used in treatment of hypertension

(drugs of choice in hypertension + diabetes mellitus), and in congestive heart failure.

15-Digitalis (cardiac glycosides): inhibit Na^+/K^+ ATPase (Na^+ pump),
used in treatment of heart failure.

16-Bipyridines: *e.g.* amrinone , milrinone , eroximore , inhibit P.D.E type iii (3),
used in resistant heart failure as short term therapy.

17-Proton pump inhibitors: *e.g.* dmeprazole, lansoprazole. Inhibit H^+/K^+ ATPase
(proton pump) in parietal cells, used as antisecretory ($\downarrow$ HCl) in treatment of peptic ulcer.

18-Allopurinol: xanthine oxidase inhibitors, $\downarrow$ uric acid synthesis in prophylaxis of gout.

19- MAO Inhibitors.

20-peripheral dopa-decarboxylase inhibitors (PDDI)

e.g. carbidopa and beuserazide, combined with L-dopa in treatment of Parkinsonism.

21- COMT-Inhibitors: tolcapone and entacapone, given with L-dopa/
carbidopa in treatment of Parkinsonism.

22-Sodium valproate and vigabartin:

Inhibit GABA transaminase, used in epilepsy (broad-spectrum anti epileptics).

23-B-lactamase inhibitors:

e.g. clavulanic acid, sulbactam and tazobactam, combined with penicillin to treat
 β -lactamase producing bacteria *e.g.* staph.

24-Cilastatin:

inhibits dipeptidase enzyme in renal cells to inhibit metabolism of imipenem into nephrototoxic metabolite (imipenem + cilastatin = tienam).

25-sulphonamides:

inhibit dihydropteroate enzyme → ↓ synthesis of dihydrofolic acid from PAPA by bacteria.

26-Trimethoprim

27-pyrimethamine

28-proguanil:

29-Methotrexate: *anticancer, inhibits dihydrofolate reductase, causes megaloblastic anemia, treated by folinic acid (= leukovorin).*

30-Rifampicin: *inhibits DNA-dependent RNA polymerase.*

31-Quinolones and fluroquinolones: *inhibits DNA-gyrase.*

32-Acyclovir: *Antiviral inhibits DNA polymerase.*

33-Zidovudine: *Antiviral, used in treatment of AIDS, inhibits reverse transcriptase enzyme.*

B- Drugs that inhibit phosphodiesterase enzymes

(P.D.E Inhibitors)

1-Selective α 1-blockers

(e.g. prazosin , they do not cause reflex Tachycardia as they increase cAMP & cGMP)

2-Bipyridines

(Amrinone , Milrinone , Enoximone) :Inhibit PDE III (3)

3-Methyl Xanthines

(Aminophylline , caffeine , theophylline , theobromine): Inhibit PDE IV (4)

1 -Sildenafil (Viagra®), ***Tadalafil*** , ***Valdenafil*** used in erectile dysfunction : Inhibit PDE V (5)

2 -Dipyridamole : anti platelet

Drugs & GIT

A- Drugs causing Hepatotoxicity

1. α -methyl dopa

(α 2-agonist-antiadrenergic-used in treatment of hypertension, is the drug of choice in hypertension during pregnancy).

2. **Dantrolene** direct skeletal muscle relaxant, ↓ Ca release from sarcoplasmic reticulum, (life-saving in malignant hyperthermia and neuroleptic malignant syndrome, given I.V).

3. **Statins e.g** ; simvastatin (anti-hyperlipidemics).

4. **Fibrates e.g** ; clofibrate (anti-hyperlipidemic).

5. Toxic doses of paracetamol

or if given with HME inhibitors as alcohol and phenobarbitone) due to accumulation of NABQI.

6. **Colchicine** (anti-inflammatory in gout).

7. **Tolcapone** (COMT-inhibitor used in parkinsonism with L-dopa).

8. **Phenytoin** (anti-epileptic+anti-arrhythmic).

9. Oxazolidinediones (*anti-epileptic in petit-mal epilepsy*).

10. Sodium Valproate (*broad-spectrum antiepileptic*).

11. MAO-inhibitors (*anti-depressants*).

12. Halothane (*inhaled general anaesthetic*).

13. Tetracyclines (*antibiotics*).

14. Sulphonamides (*anti-bacterial*).

15. Isoniazid.

16. Pyrazinamide.

17. Ethionamide.

18. Para-amino-salicylic acid.

19. Ketoconazole.

20. Griseofulvin.

21. Cis-platin (*anti-cancer*).

B- Drugs causing Diarrhea

1-Parasympathomimetics: **e.g** Carbachol – Bethanecol -Neostigmine

(Stimulate M Receptors in Small Intestine)

2-Adrenergic Neurone Depressants : **e.g** Guanethidine –Reserpine

(They causes Parasympathetic Predominance)

3-Dantrolene which is direct skeletal muscle Relaxant

4- Oral Iron : **e.g** Ferrous Fermanate & Gluconate ,

May cause black or bloody diarrhea (Some oral iron causes constipation)

5-Magansium Oxide -Hydroxide -Trisilicate : *used as Chemical antacids*

6-Metoclopramide : *Antemitic & Prokinitic*

7-Domperidone: *Antiemetic & Prokinitic*

8-Purgatives (chemical & physical)

9-Colchicine : *used in Acute gouty arthritis, may causes bloody diarrhea*

10- Erthromycin : *Anthmicrobial (Diarrhea is due to prokinetic*

11-Broad Spectrum Antimicrobials (especially if not completely absorbed)

e.g Ampicillin –Tetracyclines- Chloramphenicol –Cephalosporins

(Due to Superinfection)

12-PG-Analogues : **e.g** Misoprostol (see Peptic ulcer)

C- Drugs Causing Constipation

1-Antimuscarinic Drugs (Anticholinergic Drug = Parasympatholytics)

e.g: Atropine – Hyoscine - Antisecretory – Antispasmodic – Atropine substitutes

2-Opioid Analgesics: *e.g*

Morphine – Mepridine – Loperamide - diphenoxylate

(note that loperamide and diphenoxylate are not analgesics) they stimulate opioid receptors in GIT

3-Aluminum Hydroxide Gel : *Act as Chemical & physical Antacid*

4-Calcium Carbonate : *chemical Antacid*

5-Calcium channel blockers : *e.g Nifedipine - Verapamil*

6-Drugs Having marked

” Atropine-like Action”; e.g

- 1st Generation (= sedating) Anti-histaminics as Diphenhydramine
- Disopyramide : class I-Anti-arrhythmic
- Tricyclic anti-depressants as imipramine
- Carbamazepine : Anti-epileptic

D- Drugs Causing Nausea & Vomiting

1-Opioid Analgesics : e.g Morphine ,Methadone ,Meperidine

2-Cardiac Glycosides (Digitalis) :e.g Digoxin ,digitoxin

3-Methylxanthin : e.g Aminophylline , Theophylline

4- D2-Agonists : e.g L-Dopa , Bromocriptine

5-Estrogen (oral contraceptive) causes mainly nausea

6-Cancer chemotherapy

E- Drugs causing Allergic Cholestatic Hepatitis

1. ***Carbamazepine*** (*anti-epileptic*).
2. ***Tricyclic antidepressants*** (*TCA's*).
3. ***Chlorpromazine*** (*anti-psychotic*).
4. ***Erythromycin*** (*antibiotic*).
5. ***Chlorpromazine*** (*anti-diabetic*).
6. ***Oral contraceptives***.
7. ***Rifampicin*** (*anti-T.B*)
8. ***H2-blockers as Cimetidine*** (*anti-ulcer*).

F- Drugs activated by gastric acidic medium

1-Chlorazepate (*Benzodiazepine: anxiolytic & hypnotic*)

2-Proton Pump Inhibitors

e.g. Omeprazole

(Antisecretory drugs used in treatment of peptic ulcer)

3-Sucralfate (*mucosal protective agent, used to prevent recurrence*)

N.B.:

Ketoconazole (Antifungal)

absorption increases in acidic medium

G- Drugs destroyed by gastric acid

1-Acid-sensitive penicillins

(e.g. benzyl penicillin, procaine penicillin, benzathine penicillin, methicillin, cabencillin, ureido-penicillins)

2- Erythromycin

(to protect against HCL, erythromycin is given as enteric-coated tablets, or estolate ester is added to erythromycin)

H- Drugs destroyed by proteolytic enzymes

(Not effective orally)

1- Polypeptide antibiotics: Bacitracin & Polymixins

2- Polypeptide hormones:

e.g. Insulin, Growth hormone, Glucagon, ACTH, ADH (vasopressin)

Cardiovascular system

A- Drugs Causing Bradycardia

1-β-blocker: *e.g* Propranolol ,Nadolol , Atenololetc

2-Parasympathomimetics (Muscrinic Agonists):*e.g* Methocholidine ,Carbachol ,...

3-Digitalis (The Earlist manifestation of toxicity are nausea & vomiting + Bradycardia below 60 beats /min)

4- α1-Agonists causes reflex Bradycardia

(α1 stimulation → V.C → increase B.P → reflex bradycardia through baro receptors action)

5-General Anesthesia : *e.g* Halthone due to increase vagal tone

6-Some calcium channel blockers :

e.g Verapamil (due to Blocking Voltage-gated Ca channels in heart)

B- Drugs causing Postural Hypotention

(Orthostatic Hypotention OR Syncope)

1-Nitrates as Nitroglycerine (used in treatment of Angina pectoris)

2- α 1-blockers

(phentolamine , phenoxybenzamine , BUT selective α 1-blockers as prazosine cause “1st dose phenomenon”)

3-Ganglion blockers

(they cause Atropine like side effect + postural hypotention + sexual dysfunction in males)

4-Adrenergic neurone blockers: *(Guanithidine , reserpine , α -methyl dopa which causes minimal hypotension)*

C- Drugs used in treatment of Postural Hypotention

1. **Noradrenaline** (IV infusion) **Catecholamine**
2. **Ephedrine** (oral & IV)
3. **Phenylephrine** (oral & IV) **Non-catecholamine**
4. **Methoxamine** (oral & IV)
5. **Midodrine** (oral)

N.B. : - All previous drugs are α_1 -agonists

-They are given by I.V. injection in case of “Acute” postural hypotension due to spinal anesthesia

-They are given orally (except noradrenaline) in case of “chronic” postural hypotension

D- Drugs used in treatment of PVD

1. **α_1 -blockers** (except ergotamine , ergotoxine , dihydroergotamine , yohimbine)
2. **β_2 -Agonists** (e.g. Nylidrin , isoxsuprine)
3. **M_3 -Agonists** = parasympathomimetics (e.g. Methacholine)
4. **Calcium channel blockers** e.g. Nifedipine
5. **PGI₂** : Epoprostenol
6. **Dihydroergotoxine** (the only ergot alkaloid useful in PVD)

E- Drugs contraindicated in PVD

1. **α_1 -Agonists**
2. **Ergot alkaloids** (except dihydroergotoxine)
3. **Non selective β -blockers**

F- Drugs used in treatment of paroxysmal atrial tachycardia (PAT)

1. *B-blockers*

2. *M2-Agonists* (*e.g* Methacholine , Edrophonium , Neostigmine)

3. *Digitalis* (*cardiac glycosides*)

4. *Anti Arrhythmic drugs* : *quinidine , Ca²⁺-channel blockers (e.g. verapamil)*

5. *a1-Agonists*: *e.g. Noradrenaline , phenylephrine , Methoxamine (causes reflex bradycardia following elevation of blood pressure & contraindicated in hypertensive patients)*

G- Drugs contraindicated in PAT

- 1. β_1 -Agonists:** *e.g.* Adrenaline , isoprenaline , ephedrine
- 2. M_2 -antagonists:** *e.g.* Atropine , Gallamine
- 3. α_1 -antagonists:** *due to hypotention followed by reflex tachycardia (except selective α_1 -blockers as prazosin)*
- 4. Arteriodilators** (*e.g.* Hydralazine , Minoxidil , β_2 -agonists *due to reflex tachycardia following hypotention*)

(Atropine is non-selective muscarinic antagonist whereas Gallamine is a competitive neuromuscular blocker that block Nm receptors and also blocks cardiac M_2 - receptors)

H- Drugs causing Tachycardia

1- B1-agonists : **e.g.** Adrenaline , Isoprenaline , Ephedrine

2- B2- agonist : **e.g.** Salbutamol , Ritodrine

B2-stimulation lead to :V.D :dcrease B.P :reflex tachycardia & may be due to B1 stimulation by large doses because Selectivity is not absolute

3-Atropine (antimuscarinic = parasympatholitic) ,

note that atropine may Cause initial bradycardia due to block of presynaptic M-receptors that cause increasing release of acetylcholine or due to stimulation of C.I.C

4-Methylxanthines : **e.g.** Aminophylline , theophylline , by inhibition of P.D.E type 4 & increase C-AMP

5-Arteriodilators : **e.g.** nifedipine (and other dihydropyridine Ca^{2+} Chanel blockers) , hydralazine , minoxidil , (nitrates are mainly Venodilatores but may cause arteriodilatation) .
Arteriodilators Cause reflex tachycardia

6-Glucagon hormone (increase C-AMP by stimulation of adenylcyclase)

7-Alpha 1-blockers : **e.g.** phentolamine , phenoxybentamine , they cause reflex tachycardia due to arteriodilatation , note that selective alpha1-blockers as prazosin cause no (or minimal) tachycardia.

8-Ganglion blockers : **e.g.** Trimethaphan

I- Drugs causong hypokalemia

1-Thiazide diuretics

2-Loop diuretics

3-C.A. Inhibitors

4-Steroids (Aldosterone - cortisone)

5-Adrenaline (and other drugs acting as β_2 -Agonists) due to uptake of K^+ from blood into skeletal muscles.

J- Drugs causing hyperkalemia

1 K⁺-sparing diuretics

2 ACE-Inhibitors (*Captopril ,*)

3 ARBs (*Losartan ,*)

4 Drugs that inhibit Aldosterone synthesis (*e.g. Metyropone , see hormones*)

5 Succinylcholine

6 Non-selective B-Blocker (*e.g. propranolol*)

N.B. *Digitalis does not cause hypokalemia , but hypokalemia induces digitalis toxicity.*

K- Drugs that are contraindicated in porphyria

1-Barbiturates (*phenobarbitones , thiopentone ...*)

2-Primidone (*antiepileptic , partially metabolized into phenobarbitone*)

3-Eriseofulvin (*antifungal used for treatment of muco-cutaneous fungal Infection*)

4-Chloroquine (*anti-malarial + anti -ameobic + anti-giardiasis + anti-inflammatory in R.A .*)

Nervous system

A- Therapeutic uses of sympathomimetics

1. Shock :

Adrenaline is life-saving in anaphylactic shock , Dopamine in hypovolemic & cardiogenic shock , Dobutamine in cardiogenic shock(in Hypovolemic shock fill up then open up)

2.Acute attacks of bronchial asthma :

Adrenaline , isoprenaline (non selective) salbutamol ,terbutaline , fenoterol , reproterol (short acting selective B2 agonists)

3.Prophylaxis of Bronchial asthma : Ephedrine (non selective & CNS stimulant) , Hexoprenaline & Isoetharine (catecholamines) -selective B2-agonists , Salmeterol & formoterol (long acting selective B2-agonists)

4.Peripheral Vascular Diseases (PVD)e.g. Raynauld's diseases Nylidrin , Isoxsuprine

5.Uterine relaxants (tocolytics) in contraction ring of the uterus , premature labor , threatened abortion , dysmenorrhea : Ritodrine, salbutamol , isoxsuprine : Selective B2-agonists Adrenaline : Non-selective

6. Vasopressors in treatment of hypotension (see above)

7. Nasal decongestants :

Naphazoline ,tetrahydrozoline,xylometazoline , phenyl propanolamine , ephedrine (causes rebound congestion) , pseudoephedrine , phenylephrine , methoxamine

8. AV block (Heart block) : Isoprenaline (S.L.) , Dobutamine (I.V. infusion)

9. Nocturnal Enuresis : Ephedrine

10. Narcolepsy (Hypersomnia): Amphetamine

11. Attention Deficit Hyperkinetic Disorder (ADHD) : Methylphenidate , Amphetamine

12. Anorexigenic drugs in obesity : phenmetrazine , diphenmetrazine , diethylpropion , amphetamine (not used)

13. Acute heart failure : Dopamine , Dobutamine , Dopexamine : I.V. infusion

14. Chronic heart failure : Prenaterol (oral)

15. Glaucoma (open-angle): Adrenaline, Dipivefrin (prodrug, better than adrenaline)

16. Cardiac resuscitation in cardiac arrest : Adrenaline (intra cardiac)

17. Mydriatics for fundus examination: (α 1-agonists as Ephedrine-Phenylephrine)

18. Paroxysmal atrial tachycardia : (α 1-agonists as phenylephrine)

19. Hemostatics in cases of bleeding

As Epistaxis but not in hypertensive patients
(adrenaline-ephedrine-phenylephrine-methoxamine)

20. To prolong duration of local anesthetics

but not in fingers , toes & circumcision : Adrenaline , Ephedrine , phenylephrine , methoxamine

21 .Acute hypoglycemia due to overdose of insulin or oral hypoglycemic drugs:

Adrenaline (I.V. glucose is better)

B- Drugs causing Convulsions (Seizures)

1-CNS stimulants:

a-Methylxanthines (Theophylline)

b-Amphetamine

c-Cocaine

d- Atropine

e-Araleptics (brain stem stimulants)

f- Strychnine (spinal cord stimulant)

2- Morphine *(by decrease release of GABA)*

3-Meperidine *(metabolized into normeperidine +atropine like action)*

4-Aspirin *(acute toxicity) due to increase Glutamate /GABA ratio*

5-Chlorpromazine *(major tranquilizer = Antipsychotic = Neuroleptic)*

6-MAO-inhibitors

7-Lithium (*anti-manic, mood stabilizer in bipolar disorders*)

8-Penicillins (*if large dose or intrathecal injection*)

9-Carapenem **e.g.** Imipenem (*B-lactam antibiotics*)

10-Cycloserine (*antibacterial _ inhibits cell wall synthesis*)

11-Fluoroquinolones *especially with NSAIDS & theophylline*

12-Amphotericin B (*polyene –antifungal*)

13-Oxamniquine (*Anti bilharzial*)

14-Cardiac glycosides

C- Drugs causing psychosis

1-D2-Agonist *e.g.* L-dopa , bromocriptine (antiparkinsonian drugs)

2-Indomethacin (NSAID)

3-Glucocorticoides

4-Cycloserine

5-Cardiac glycosides

D- Drugs causing Depression

1- Estrogen (*oral contraceptives*)

2-Reserpine (*adrenergic neurone depressant, depletes the brain from monoamines
:5HT, noradrenaline & dopamine*)

3- Alpha -methyldopa (*decrease synthesis of monoamines by decrease dopa decarboxylase*)

4-Chlorpromazine (*causes pseudo-depression*)

Urinary system

A- Drugs causing Nephrotoxicity

1-NSAIDs except paracetamol (cause "**analgesic nephropathy**" due to renal V.C. by
↓ PGE and PGI synthesis.

2-Colchicine (+ hematuria).

3-Gold salts (in treatment of **rheumatoid arthritis**).

4-Vancomycin.

5-Aminoglycosides.

6-Cephalosporins.

7-Methicillin.

8-Sulphonamides.

9-Tetracyclines (especially of expired = Fanconi syndrome).

10-Amphotericin B (Anti-fungal).

11-Acyclovir (Anti-viral).

12-Demeclocycline (Anti-bacterial tetracycline).

13-Lithium (Anti-manic + mood stabilizer).

14-Methoxyflurane (inhalant general anaesthesia as halothane).

B- Diuretics causing Hypokalemia

- 1 **Thiazide diuretics** (*e.g.* hydrochlorothiazide)
- 2 **Loop diuretics** (*e.g.* furosemide, ethacrynic acid)
- 3 **Carbonic anhydrase inhibitors** (*e.g.* Acetazolamide, methazolamide)

C- Diuretics causing hyperkalemia = K⁺ sparing diuretics

- 1 **Spironolactone** Aldosterone antagonists
- 2 **Canrenone**
- 3 **Trimetaphane** Non-Aldosterone antagonists
- 4 **Amiloride**

D- Diuretics causing alkalosis

- 1-**Thiazide diuretics**
- 2-**Loop diuretics**

E- Diuretics causing acidosis

- 1 K⁺ sparing diuretics***
- 2 Carbonic anhydrase inhibitors Cause hyperchromic acidosis***
- 3-Acidifying diuretics (NH₄Cl)***

F- Self – limiting diuretics

They cause acidosis leading to reabsorption of Na⁺ in exchange for H⁺ or NH₄⁺

- 1 Carbonic anhydrase inhibitors***
- 2 Acidifying diuretics***

G- Diuretics causing hypercalcemia

- 1-Thiazide diuretics***
- 2-Non-aldosterone antagonists***

H- Diuretics causing hypocalcemia

- 1 Loop diuretics***
- 2 Spironolactone (Aldosterone antagonist)***

Teratogenic drugs

1-NSAIDs except paracetamol (*Aspirin causes cardiac septal defect, but is the safest NSAID*).

2-Benzodiazepines.

3-Barbiturates.

4-Chlorpromazine (*phenothiazine antipsychotic and anti emetic*).

5-Lithium.

6-ACE-inhibitors *e.g.* Captopril.

7- AT1_(Angiotensin) receptor-antagonists *e.g.* Losartan.

8-Antihistaminics *e.g.* Cyclizine and Meclizine.

9-Oral anticoagulants *e.g.* Warfarin.

10-Thiazide and Loop diuretics.

11-Phenytoin.

12-carbamazepine.

13- Sodium valproate: *antiepileptic, causes spina bifida.*

14-Nitrous oxide *(inhaled gas general anesthetic).*

15-Sodium nitroprusside *(mixed vasodilators given I.V. infusion)*

16-Aminoglycosides → *fetal deafness.*

17-Tetracyclines.

18-Sulphonamides → *hyperbilirubinemia and kernicterus.*

19-Quinolones → *damage of growing cartilage and arrest of growth.*

20-Griseofulvin *(antifungal).*

N.B.

1-Morphine *is not teratogenic but cause "fetal Addiction".*

2-Thalidomide *was used as anxiolytic / hypnotic and it caused*

"Amelia" = absent limbs and "phocomelia" = short limbs (thalidomide catastroph)

Prodrugs -- Active drugs---Active metabolite

Prodrugs :

- 1 Inactive drugs converted in the body into active metabolites.*
- 2 Activation usually occurs in the liver.*
- 3 Chlorazepate is converted into active metabolite nordiazepam in the stomach by gastric acid.*

Examples :

1-Dipivefrin (used in glaucoma).

2-Phenoxybenzamine (α -blocker).

3-Hexoprenaline

(selective β_2 agonist used in bronchial asthma, it is a non-catecholamine, converted to active metabolite by COMT).

4-Minoxidil (antihypertensive, converted into minoxidil sulphate).

5. Enalapril, Fosinopril, Ramipril (ACE inhibitors).

6. Proton pump inhibitors, e.g; Omeprazole (in treatment of peptic ulcer).

7-Cortisone is converted into cortisol (= hydrocortisone).

8-Sulindac and Nabumetone (NSAID).

9-Ampicillin esters(= pro-ampicillins) as Bacampicillin, Pivampicillin, Talampicillin, converted into ampicillin in liver and GIT mucosa.

10-Chlorazepate (Benzodiazepine).

11-Propacetamol → Paracetamol, given by injection.

Active drugs converted into active metabolites

1. **Phenacetin** → Paracetamol = Acetaminophen (analgesic-antipyretic).
2. **Benzodiazepines** except LOT – Nitrazepam - Clonazepam.
3. **Morphine** → Morphine-6-glucuronide.
4. **TCA's e.g;** Imipramine → Desipramine, Amitriptyline → Nortriptyline.
5. **Spironolactone** → Canrenone (Aldosterone-antagonist K-sparing diuretic).

Iatrogenic diseases

Drug-induced Diseases

Disease	Drugs
1- peptic ulcer	- NSAIDS (except paracetamol) - Glucocorticoids
2- Bronchial Asthma	- NSAIDS (except paracetamol) - Morphine - Non-selective B-blockers (propranolol) - Muscarinic agonists, e.g: Methacholine, Carbachol, Neostigmine
3- Hypertension	- Glucocorticoids - oral contraceptives - Alpha1-agonists (adrenaline-noradrenaline, phenylephrine-ephedrine, phenylpropranolamine)

4- Angina pectoris	- B1-agonist (adrenaline-isoprenaline) - Thyroid hormones - Methyl xanthines - Arteriodilators (hydralazine,minoxidil,nifedipine....) due to reflex tachycardia
5- Glaucoma	- Atropine – Hyoscine - Atropine substitutes - Atropine- like drugs - ganglion blockers - vasodilators (e.g:nitrates) - Glucocorticoids
6- Systemic Lupus Erythematosus (SLE)	- Hydralazine (arteriodilator used as anti hypertensive) - Procainamide (class I.A anti arrhythmic) - Isoniazid (anti T.B) (They cause iatrogenic SLE especially in slow acetylators)

7- Parkinsonism	- D2-blockers (e.g:phenothiazines as Chlorpromazine,butyrophenones as haloperidol,metoclopramide) - Reserpine - Alpha-methyl dopa
8- Cushing Syndrome	- Glucocorticoides (given systemically for long duration)
9- AV block (Heart block)	- Digitalis - verapamil - B-blockers - Methacholine
10- Tinnitus Vertigo	- Salicylates (tinnitus I the most important manifestation of salicylism) - Ototoxic drugs,e.g:loop diuretics, aminoglycosides,vancomycin - Metronidazole – Minocycline - Indomethacin and phenylbutazone

Drugs used for diagnostic tests

Drug	Diagnosis of
1-Phentolamine (non-selective α -blocker)	Sustained type of pheochromocytoma (Phentolamine cause severe hypotension in these patients). "Regtivity test"
2-Clonidine (central α_2 -agonist)	Sustained type of pheochromocytoma = clonidine suppression test (Clonidine can't suppress release of catecholamines from the tumor)
3-Methacholine (M-agonist) 4-Histamine (Autacoid)	Paroxysmal type of pheochromocytoma = provocative test (they cause hypertension in patients with pheochromocytoma instead of hypotension in other patients)
5-Ergotamine (Ergot alkaloid-oxytocic-weak α_1 -agonist)	Prinzmetal (variant or vasospastic) angina. (Ergotamine causes marked coronary V.C. in these patients)

6-Adrenaline <i>(sympathomimetic-catechol amine-β and α agonist)</i>	<i>Acute hemorrhagic pancreatitis (Lewi's test). (Adrenaline causes active mydriasis in this case)</i>
7-Methacholine (M-agonist)	<i>Bronchial asthma = provocative test (Methacholine causes marked bronchospasm and inc. bronchial secretion in these patients)</i>
8-Edrophonium I.V. 9-Neostigmine I.M. + Atropine <i>(Edrophonium and neostigmine are reversible anti - cholinesterases)</i>	<i>Myasthenia gravis</i>
10-Edrophonium I.V.	<i>Differentiation between myasthenic and cholinergic crisis in patients of myasthenia gravis.</i>
11-Ampicillin	<i>Infections mononucleosis (Ampicillin causes maculopopular rash).</i>

Acute toxicity of the drugs

Drugs causing toxicity	Signs and symptoms of acute toxicity (overdose)
1-Amphetamine 2-Cocaine	<i>Hallucinations (shizophrenia-like) – convulsions – hypertension – active mydriasis – coma and finally inhibition of R.C.</i>
Ergot alkaloids (Ergotism) <i>due to overdose of ergotamine or eating rye grains infected by ergot fungus.</i>	<i>Mania – hallucinations – convulsions -hypertension followed by hypotension –hyperpyrexia – bradycardia – nausea & vomitting – coma and finally inhibition of R.C.</i>
Organophosphorus compound poisoning.	<i>Bradycardia – hypotension – bronchospasm and increased bronchial secretion – excessive secretion – diarrhea – urination – miosis – skeletal muscle twitches followed by paralysis – convulsions – followed by coma and inhibition of R.C.</i>

Atropine	<i>Mania – hallucinations – convulsions – hypotension – tachycardia – passive mydriasis – dry hot skin (flush & fever) – constipation – urine retention – finally coma and inhibition of R.C.</i>
Competitive neuro - muscular blockers as curare	<i>Apnea (due to paralysis of respiratory muscles) – hypotension – tachycardia – bronchospasm</i>
Morphine (see CNS)	<i>Coma + inhibition of R.C. + pin point pupil</i>

- 1 The cause of death in acute toxicity is due to depression of R.C., i.e central respiratory failure.
 - 2 Competitive neuro-muscular blockers cause peripheral respiratory failure but not central because they don't cross B.B.B
 - 3 Organophosphorus compound poisoning cause both central and peripheral respiratory failure.
 - 4 General rules for treatment of acute drug toxicity
 - a. Stomach wash = gastric lavage (if the drug is ingested**)
 - b. Care for respiration (endotracheal intubation – artificial respiration)
 - c. Antidote (if there is a specific antidote , e.g. atropine for organophosphorus poisoning , neostigmine for curare toxicity , physostigmine for atropine poisoning)
 - d. Symptomatic treatment (e.g. anticonvulsant as diazepam)
 - e. Increase (promote) renal excretion of the drug (by changing pH of urine : Acidification of urine in toxicity of basic drugs as amphetamine and ephedrine using ammonium chloride or ascorbic acid , Alkalinization of urine in toxicity of acidic drugs as salicylates (aspirin) using NaHCO_3 . The drug should be completely or partially excreted in urine unchanged)
- **** In acute morphine toxicity stomach wash is performed although morphine is given by I.V. injection!! (see CNS) **N.B** : The size of the pupil is a useful diagnostic sign.

** Therapeutic uses of choline esters*

<i>Choline esters include:</i>	<i>Therapeutic uses:</i>
1-Acetylcholine (natural)	<i>None (must be given I.V. – very short duration – non-selective M-agonist)</i>
2-Methacholine	<i>1.Provocative test in diagnosis of bronchial asthma</i> <i>2.P.V.D.</i> <i>3.P.A.T</i> <i>4.Provocative test in diagnosis of paroxysmal type of pheochromocytoma</i>
3-Carbachol 4-Bethanechol	<i>1.Glucoma (eye drops)</i> <i>2.Non-obstructive post-operative paralytic ileus</i> <i>3.Non-obstructive post-operative (or post-partum) urine retention</i>
5-Succinylcholine <i>(Depolarizing neuro – muscular blocker)</i>	<i>1.Adjuvant to general anaesthesia</i> <i>2.Endotracheal intubation</i>

N.B. : - All except Acetylcholine are synthetic.

- All are quaternary ammonium compounds.
- All except succinylcholine are parasympathomimetic.

Causes & Examples of Cross allergy

1-Similarity in the chemical structure of different drugs e.g.

- Penicillins & Cephalosporins
- Sulphonamides & thiazide diuretics, loop diuretics, Carbonic anhydrase inhibitors, & Sulphonylureas.

2- Similarity in the mechanism of action e.g.

- Aspirin & other NSAIDS (except paracetamol) : Bronchial asthma

Drugs that should never be stopped SUDDENLY (abruptly)

1. ***β-blockers*** : sudden withdrawal causes rebound tachycardia , arrhythmia , angina & even acute myocardial infarction
2. ***Clonidine*** (and other selective α_2 -agonists) : sudden withdrawal causes “rebound hypertension” which is treated by giving clonidine again or by α_1 - blocker $\pm$ β -blocker or labetalol but never use non-selective β -blocker alone
3. ***Noradrenaline IV infusion*** : sudden withdrawal cause “rebound hypotension”
4. ***Corticosteroids*** : sudden withdrawal after chronic use causes “Acute Addisonian crisis”

Drugs and pheochromocytoma

Drugs used in treatment of pheochromocytoma (If inoperable)

- 1 **α 1-Blockers** , especially phenoxybenzamine because it is a non-competitive irreversible blocker and is the most potent α -Blocker.
- 2 **Labetalol** (β_1 + α_1 Blocker).
- 3 **β -Blockers** may be added to α -Blocker but never use non-selective β -Blockers (as propranolol) Alone as they cause more hypertension due to unopposed α -effect.

N.B. α -blockers may be also used pre-operative and intra-operative to avoid elevation of B.P during excision of pheochromocytoma.

Drugs used in diagnosis of pheochromocytoma

1. **α -Blockers** as phentolamine (Regitine test) Marked in B.P in sustained pheochromocytoma.
2. **Clonidine** (Clonidine suppression test) can't release of catecholamines in sustained pheochromocytoma.
3. **Methacholine and Histamine** release of catecholamines of B.P (instead of hypertension in other patients).
This is a "Provocative test" which is obsolete.

Drugs contraindicated in pheochromocytoma

1. **Guanethidine** inhibit uptake¹ of noradrenaline sustained action of noradrenaline on post-synaptic α_1 -receptors on B.Vs mor in B.P
2. **Non-selective β -Blockers** if used alone (see before)
3. **α_1 -Agonists**

Drugs and body characters

A- Drugs causing alopecia

- 1- Anticancer drugs.*
- 2- Heparin (anticoagulant).*
- 3- Colchicine (treatment and prophylaxis of acute gouty arthritis).*
- 4- Sodium Valproate (broad spectrum antiepileptic).*
- 5- Oxazolidinediones (antiepileptics in petit-mal epilepsy).*
- 6- Interferons (in treatment of Hepatitis C virus "HCV").*

B- Drugs used in treatment of alopecia

1 .Minoxidil sulphate

2.Pilocarpine

C- Drugs causing hirsutism

1- Androgens.

2- Progesterone (in contraceptive pills).

3- Phenytoin (antiepileptic).

N.B: Minoxidil causes "Hypertrichosis".

D- Drugs causing Gynecomastia

1-Digitalis (due to steroid structure)

2-Spironolactone (due to steroid structure)

3-Reserpin Due to decrease dopamine in CNS increase prolactin

4- α -methyl dopa

5-Ketoconazole (antifungal , decrease synthesis of androgens)

6-Cimetidine (H_2 -blocker , used in treatment of peptic ulcer , causes anti-androgenic action)

7-Estrogen (given to males for treatment of cancer prostate)

Drug groups

- zoline group

α_1 -Agonists, used locally as nasal decongestants

1 Naphazoline

2-Tetrahydrozoline

3-Xylometazoline

4 **Tolazoline**... non-selective competitive α -adrenergic receptor antagonist, causes nasal congestion

- lol group:

1- β -Blockers (Propranolol-Nadolol-Atenolol-Esmolol-.....)

(Butoxamine is selective β_2 -Blocker)

- zosin group = selective α_1 -blockers

1-Prazosin

2-Terazosin

3-Doxazosin (Tamsulosin = selective α_{1A} -blocker used in prostatic hyperplasia)

- nidine group = α 2-Agonists

- 1 **Clonidine** (*anti hypertensive*)
- 2 **Apraclonidine** (*Used in glaucoma*)
- 3 **Brimonidine**
- 4 **Tizanidine** (*central skeletal muscle relaxant*)

- zepine group = selective M1-blocker
(*useful in treatment of peptic ulcer*)

- 1-**Pireuzepine**
- 2-**Telenzepine**

- stigmine = carbamates , reversible anticholine-esterases :

- 1-**Physostigmine**
- 2-**Rivastigmine** (*in Alzheimer*)
- 3-**Neostigmine** (*In myasthenia gravis*)
- 4-**Pyridostigmine**

- triptan group

used in acute migraine headache , agonists on 5HT_{1D}

1-Sumatriptan

2-Rizotriptan

3-Zolmitriptan

4-Ranitriptan

- tropium group

= Atropine substitutes in bronchia asthma

1-Ipratropium

2-Oxytropium

3-Tiotropium

- tropine group = Atropine substitutes

1 Benzotropine (in Parkinsonism)

2 Homatropine Mydriatics

3 Eucatropine

- curium & curonium group = Competitive neuro-muscular blockers

1-Atracurium

2-Cis-atracurium

3-Mivacurium

4-Pancuronium

5-Vecuronium

6-Alcuronium

- tidine group = H2-Blockers used in peptic ulcer

1-Cimetidine (+ HME inhibitor + Gynecomastia and infertility)

2-Famotidine

3-Ranitidine

4-Nizatidine

- setron group = 5HT3-Antagonists

used as anti-emetics in cancer chemotherapy and radiotherapy

1-Ordansetron

2-Granisetron

3-Tropisetron

- lukast group = Leukotriene receptor antagonist

used in prophylaxis of bronchial asthma

1=Montelukast

2-Zafirlukast

- zolamide group = Carbonic Anhydrase Inhibitors

1-Acetazolamide

2-Methazolamide *See diuretics*

3-Ethoxzolamide

4-Dorzolamide *(eye drops in glaucoma)*

- *dipine* group = Dihydropyridine calcium channel blockers
(cause arteriodilatation more than cardiac dep.)

- 1-Nifedipine**
- 2-Amlodipine**
- 3-Nimodipine**
- 4-Felodipine**
- 5-Nicardipine**
- 6-Isradipine**

- *pril* group = ACE Inhibitors

- 1-Captopril**
- 2-Lisinopril**
- 3-Enalapril**

- *sartan* group = ARBs (Angiotensin-Receptor Blockers)

- 1 Losartan**
- 2 Valsartan**
- 3 Candesartan**
- 4 Telmesartan**

*- **caine** group = Na⁺ channel blockers acting as local anaesthetics*

1-Procaine

2-Tetracaine

3-Lidocaine (which is also antiarrhythmic)

Take care :

- *Butyryl choline esterase = Pseudocholine esterase*
- *Scopolamine = Hyoscine*
- *Suxamethonium = Succinyl choline*
- *Isoproterenol = Isoprenaline*
- *Epinephrine = Adrenaline*
- *Norepinephrine = Noradrenaline*

G-protein coupled receptors

G_s Stimulation of adenyl cyclase (A.C.) enzyme increase cAMP

1-All β -receptors (β_1 , β_2 , β_3)

2-H₂-receptors (in heart, parietal cells of stomach, B.Vs)

G_q Stimulation of phospholipase C (PLC)

increase Diacyl glycerol (DAG) and inositol triphosphate (IP₃) increase Ca²⁺ spasmogenic

Except in endothelium of B.Vs release of nitric oxide increase cGMP V.D.

1 α_1 -receptors

2 M₁-receptors

3 M₃-receptors

4 H₁-receptors (in smooth muscle fibres as bronchi-B.Vs-skin)

5 5HT₂-receptors (in CNS-smooth muscle fibres as bronchi-platelets)

6 AT₁-receptors (AT II acts on AT₁-receptors V.C, increase aldosterone, increase sympathetic activity and trophic changes in heart and B.Vs)

Gi Inhibit adenyl cyclase decrease cAMP

- 1 α_2 receptors (presynaptic-CNS-inhibit renin secretion)*
- 2 M_2 -receptors (Heart-presynaptic)*
- 3 $5HT_1$ -receptors (in CNS)*
- 4 H_3 -receptors (presynaptic-CNS)*

Therapeutic uses of Ergot Alkaloids

1-Acute attack of Migraine headache : Ergotamine , Dihydroergotamine , cafergot

2- Prophylaxis of migraine headache : Methysergide (anti-serotonin)

3-Prevention & treatment of post-partum haemorrhage

*4- Involution of the uterus after delivery Ergomrine &Diagnosis of Prinzmetal
angina Methylergometrine*

5-Senile cerebrovascular insufficiency: Dihydroergotoxine

6- PVD : Dihydroergotoxine

7-Parkinsonism Bromocriptine

8-Hyperprolactinemia in males and females (D_2 -agonist that crosses BBB)